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TRANSFER OF RADIONUCLIDES FROM THE ENVIRONMENT TO HUMAN MILK - A REVIEW

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Research report

TRANSFER OF RADIONUCLIDES FROM THE ENVIRONMENT TO HUMAN MILK

ABSTRACT

The author reviews literature from an on-line bibliographic search and describes what is known about radionuclide and elemental transfer from the environment to human milk. Included in the review are factors affecting elemental transfer, element concentrations observed in human milk, as well as sampling and analytical methods used. Recommendations are given for the development of a field survey.

RÉSUMÉ

L'auteur procède à un examen de la documentation recueillie à la suite d'une recherche bibliographique informatisée et décrit ce qui est connu du transfert de radionucléides et d'éléments de l'environnement au lait maternel. Le compte rendu comprend un examen des facteurs touchant le transfert d'éléments, des niveaux de concentration observés dans le lait maternel, ainsi que les techniques d'échantillonnage et d'analyse utilisées. Enfin, l'auteur fait des recommandations pour la mise au point d'une enquête sur le domaine.

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Appendix 1

TRANSFER OF RADIONUCLIDES FROM THE ENVIRONMENT TO HUMAN MILK

A. INTRODUCTION

The objective of this project was to critically evaluate the available literature on the transfer potential of radionuclides from the environment to human milk. Because the biological characteristics of a radionuclide are generally a function of its atomic number (the chemical characteristics) rather than of its isotope number (the radioactive characteristics), the literature search emphasized the transfer of elements, stable or radioactive, from the environment to human milk. Radiopharmaceuticals were included in the review, although most are administered by routes which are not typical of environmental exposures. As there was considerable interest in survey methods, consideration was also given to sampling and analytical techniques used to assess trace element transfer.

This report presents the results of the literature review. It points out data gaps, and factors to be considered when planning a field survey to measure the concentrations of radionuclides in human milk.

B. METHODS AND RESULTS OF INFORMATION RETRIEVAL

Computer bibliographic databases selected for searching are listed in **Table 1**. They were chosen because of their comprehensive representation of relevant documents in the published literature. Their coverage includes journal articles, technical reports, monographs, theses, conference proceedings, and government documents from international sources. Search strategies were tailored to the requirements of each database, but included some combination of the following search items - human milk, mothers' milk, lactation, colostrum, radioisotope, element(s) - or appropriate search terms selected from a database's controlled vocabulary. From these searches, approximately ninety (90) references were requested in hard copy.

Of the hard copy references received, only eight assessed trace element concentrations in human milk as a function of observed dietary intake. These references have been summarized in **Appendix 1**. Approximately forty references described trace element concentrations measured in human milk. Their objectives were various, such as to compare infant intake with recommended daily allowance (Ref. 1), to compare infant intake with that which constitutes a health hazard (Ref. 2), to compare with concentrations in human milk reported elsewhere (Ref. 3), to determine geographical distribution (Ref. 4), to compare with cow's milk and infant formula (Ref. 5), to describe concentration

TABLE 1. Computer Bibliographic Databases Selected For Searching

Name	Organization	Time Span	Scope
INIS (International Nuclear Information System)	International Atomic Energy Agency, Vienna, Austria	1970 to date	The INIS database is the major source of bibliographic information in the field of nuclear science and technology. It covers approximately 95 % of the world's literature in the field. Thirteen international organizations and national centres in more than 65 countries contribute information to the database. Subject coverage includes chemistry, health and safety, isotope and radiation applications, environmental sciences and life sciences among others.
EMBASE	Excerpta Medica, Amsterdam, Netherlands	1974 to date	This file contains abstracts and citations of articles from over 4,000 international biomedical journals, and provides extensive coverage of drug, pharmaceutical, chemical, environmental and pollution literature.
ENVIROLINE	EIC/Intelligence, New York	1971 to date	ENVIROLINE provides indexing to more than 5,000 international primary and secondary source publications reporting on the environment, including government documents, industry reports, proceedings and monographs.
ENVIRONMENTAL BIBLIOGRAPHY	Environmental Studies Institute, Santa Barbara, CA.	1973 to date	ENVIRONMENTAL BIBLIOGRAPHY covers the fields of general human ecology, and nutrition and health.
POLLUTION ABSTRACTS	Cambridge Scientific Abstracts, Bethesda.	1970 to date	Environmentally-related literature is indexed in this database, including the topic of radiation.
MEDLINE	U.S. National Library of Medicine	1966 to date	MEDLINE contains literature references to over 3,000 biomedical journals published in the U.S. and 70 other countries, and includes over 4 million records to date. Citation to chapters or articles from selected monographs are also included.
BIOSIS PREVIEWS	BioSciences Information Service, Philadelphia, Pa.	1969 to date	BIOSIS provides worldwide coverage of life sciences literature, monitoring over 9,000 journals in addition to monographs, conference proceedings, theses, reports, reviews & letters. This database will be a useful resource for papers on mammalian milk.
TDB Toxicology Data Bank	U.S. National Library of Medicine	updated quarterly	TDB is composed of over 4,000 comprehensive peer-reviewed chemical records. It contains toxicological, pharmacological, environmental, occupational, manufacturing and use information, as well as chemical and physical properties.
and Technology Abstracts)	Information Service, Frankfurt, F.R.G.		journals from over 50 countries, as well as monographs. This database will provide valuable information on breast-feeding as well as components of mothers' milk, and the maternal ingestion route.
NTIS	National Technical Information Service, Springfield, Virginia	1964 to date	This database consists of government - sponsored research, development and engineering, as well as analyses prepared by U.S. federal agencies (such as Dept. of Health and Human Services, Dept. of Energy, etc), their contractors or grantees. The database also includes some foreign language materials.
International Pharmaceutical Abstracts	American Society Hospital, Pharmacists, Washington, D.C.	1970 to date	The database provides information on all phases of the development and use of drugs, by indexing 500 pharmaceutical, medical & related journals. Abstracts reporting clinical studies include the study design, number of patients, dosage, dosage forms and schedules.
Occupational Safety and Health (NIOSH).	Clearing house for Occupational Safety and Health (U.S.), National Institute for Occupational Safety and Health	1972 to date	NIOSH covers all aspects of occupational safety and health, and includes such topics as hazardous agents, unsafe workplace environment and toxicology. This database provides citations to more than 400 journal titles in addition to 70,000 monographs and technical reports.
CA Search	Chemical Abstracts Service, Columbus, Ohio.	1967 to date	Over 6 million records are contained in this database from the printed version, Chemical Abstracts. Information on analytical methods, and the gathering of milk samples will be searched for on this file.
Chemical Exposure	Chemical Effects Information Center, Oak Ridge National Laboratory	1974 to date	CHEMICAL EXPOSURE contains information on chemicals that have been identified in both human tissues and body fluids, and in feral and food animals. The database presents body burden data including human and animal exposure to food, air and water contaminants and pharmaceuticals.

changes during lactation (Ref. 6), to determine milk:plasma ratios, also called M/P ratios (Ref. 7), to determine milk:blood ratios (Ref. 8), to compare results from persons in urban and rural environments (Ref. 9, 10), to compare results from persons of different nationalities (Ref. 11), or to describe an analytical method (Ref. 12, 13). Of the remaining references received in hard copy, nine were not applicable, as they dealt with mammals other than man; ten were in foreign languages, two of which were translated for the study (Ref. 14, 15).

Because there were few papers comparing trace element concentrations in diet with those in human milk, there was insufficient data for detailed review of analytical methods or statistical evaluation of results. Instead, it was more appropriate to develop an overview of what is known about trace element concentrations in human milk, factors which influence trace element transfer to human milk, sampling and analytical methods used in previous surveys, and implications in planning a field survey. These subjects are discussed in the following sections.

C. CHARACTERISTICS OF HUMAN MILK

Human milk is a suspension of fat (1 to 4%) in a solution of proteins (0.8 to 0.9%) , carbohydrates, vitamins and minerals. The alveolar cell of the mammary gland synthesizes the fat, protein, and carbohydrate components of the milk. The vitamins and minerals are secreted into the milk.

It is well known that the magnitude of variation in human milk composition, even of milk secreted by an individual woman, is very large. Of the major constituents in human milk, the lipid fraction is most variable. The fat content of milk varies among individuals, with duration of lactation, with time of day, and during the course of a single feed. Hind milk, or milk drawn late in a feed, is rich in fat compared to that of fore milk, or milk drawn early in a feed. Therefore, estimates of infant intake of any lipid-associated substance requires careful sampling strategies to ensure representative samples.

The concentrations of individual milk proteins may also vary considerably during lactation. Until recently, milk protein has been determined by measuring the total nitrogen content. However, total nitrogen is not directly related to total protein, because of variations in levels of non-protein nitrogen constituents. Total and individual proteins are now receiving more attention, and generally have been found to vary differently from the total nitrogen. These proteins may provide binding sites for substances being transported into the milk.

Milk carbohydrate, lactose, appears to be the component in milk which is most constant in concentration. Lactose in the alveolar cell may determine water content. Human milk is isosmotic with plasma. Its average pH is 7.2 (Ref. 16).

The mammary alveolar cell may also be responsible for vitamin and mineral content of the milk, although the control mechanisms are unknown. The bioavailability of trace elements from human milk is known to be very high, possibly due to factors in the milk (as yet unknown) promoting absorption of these elements (Ref. 6). For example, absorption of zinc from human milk was found to be 41% ± 9%, in comparison to 28% ± 15% for cow's milk (Ref. 17). In human milk, zinc is bound to citrate; in cow's milk, zinc is bound to casein.

D. FACTORS AFFECTING UPTAKE BY THE MAMMARY GLAND

Although dose-response relationships are not well characterized for the transfer of trace elements to human milk, several possible transport mechanisms have been described (Ref. 7, 16): -

1. Passive diffusion processes may occur, through pores in the cell membrane for water-soluble species or through lipid components of the membranes for lipid-soluble species.

2. Active transfer processes may occur for non-polar species, with a low-density lipoprotein fraction of serum acting as a blood carrier.

3. A direct pathway may exist from capillary to interstitial space to intercellular cleft and directly into the milk.

For passive diffusion processes, the movement of substances from the blood into the milk is dependent upon the relative concentrations in the milk:plasma (M/P) compartments. For active processes, the movement of compounds from the blood into the milk is dependent upon their chemical characteristics. Key characteristics affecting chemical uptake in human milk are summarized in **Table 2**, together with examples to illustrate the effects of these factors. Several of these have been drawn from the greater knowledge of drug partitioning characteristics.

It can be seen that there are numerous factors affecting theoretical transfer of trace elements to human milk. The result appears to be transfer characteristics which are unique to each element. Transfer characteristics which have been observed for individual elements or inferred from experimental data are described in the following chapter.

Table 2. Factors Affecting Uptake Of Radionuclides or Radioactive Compounds In Human Milk

1. Molecular Weight (<200)
eg Sulfasalazine, a conjugate of sulfapyridine and 5-aminosalicylate, has a molecular weight of 398 and is not found in breast milk after ingestion. The cleavage product, sulfapryridine, is found in milk with a milk:plasma (M/P) ratio of 0.6 (Ref. 16).

2. Lipid -water solubility
eg Ethanol is a neutral, lipid soluble compound of low molecular weight. It passes readily into milk, resulting in an M/P ratio of 0.8 to 1.

3. Degree of ionization in plasma (pH 7.35) and milk (pH 7 to 7.25)
eg Erythromycin is neutral in blood (pKa of 8.8); erythromycin passes readily into milk, resulting in an M/P ratio of approximately 3. In contrast, penicillin is ionized in plasma (pKa of 2-3); penicillin has an M/P ratio of less than 0.2 (Ref. 7).

4. Ratio of Ionic strength in plasma:milk

5. Degree of protein binding in blood fractions (plasma:erythrocytes) and milk
eg Organic mercury binds efficiently to erythrocytes, and is less available for transfer to milk. In a methylmercury poisoning, the M/P ratio for total mercury was 0.03 (Ref. 18).

6. Existence of maternal body burden in adipose tissue
eg Organochlorine M/P ratios are generally 1 to10. However, concentrations in milk are similar to concentrations in adipose tissue, suggesting equilibrium between maternal adipose and milk fat (Ref. 7).

7. Interactions with other compounds/elements
eg Gallium is thought to accumulate in milk through competitive binding for calcium (Ca 2+) and magnesium (Mg 2+) binding sites (Ref. 19). Lithium, in the presence of sodium depletion, is reabsorbed by the kidney, resulting in higher serum and breast milk concentrations (Ref. 20).

8. Homeostatic Processes
eg Although calcium concentrations in milk vary greatly among women, they are almost constant for each individual and appear to be unaffected by diet (Ref. 21). Iron concentrations in the milk of mothers with a good iron status do not increase with increased dietary iron (Ref. 11). On the other hand, increased intakes of sodium (in food) or iodine (in food or from external application) are reflected rapidly in breast milk (Ref. 21, 22).

9. Relative concentrations of stable:radioactive isotopes in maternal body fluids/tissues.

E. ELEMENT TRANSFER TO HUMAN MILK

The uptake of any element by the mammary gland is partly a function of the element's chemical characteristics. Therefore, this chapter has been organized by chemical groups on the chemical periodic table (elements with similar properties). Information has been summarized on 25 elements. Of these, only one (lead) is a member of the uranium or thorium decay series. No information was found on the occurrence in human milk of other members of the series.

1. Halogens

The halogens are those elements in group 7A of the periodic table, and include chlorine, bromine, and iodine. Only information on iodine was found.

1.1 Iodine (I)

Iodine is an essential nutritional element with a recommended dietary allowance of 40 mg/day. There is a broad variation of iodine concentrations in human milk (29 to 490 ug/L, mean 178 ug/L in Ref. 25, 23 to 296 ug/kg in Ref. 1, 8 to7000 ug/L in Ref. 26), with high concentrations associated with reported consumption of iodized salt or algae (although actual consumptions were not given). Topical applications of an iodine medication were observed to result in total iodine M/P concentrations of 8 and inorganic iodine M/P concentrations of 25 (Ref. 22). The iodine concentration of human milk has been observed to increase within five minutes of iodine ingestion (Ref. 21). However, no significant difference could be found in milk collected at the beginning and end of feeds or from left or right breast (Ref. 1).

Not surprisingly, intravenous administrations of radioactive iodine pharmaceuticals (eg I-131 labelled macroaggregated human serum albumin or MAA for lung scans) have resulted in increased milk radioactivity levels. Peak levels occurred approximately 20 to 24 hours after administration in two cases described by (Ref. 27), but the total activity was ten times higher in the sample from the third day lactation than in the sample from the third month lactation. The lower activity in the third month lactation may have been due to a larger volume milk production. After I-131 labelled tracers have been given to a lactating woman, recommendations are given to interrupt nursing for 7 to 14 days to minimize the dose contribution to the breast-feeding infant.

When radioactive iodine pharmaceuticals have been used, a post-injection course of potassium iodide has been administered to reduce thyroid uptake of the radioactive isotope. A similar strategy has been considered as an emergency measure for radioactive fall out. One milligram of iodide administered daily to children three years old and less blocked thyroid uptake of therapeutic I-131 by 95% (Ref. 28). There is no

evidence that the mammary gland secretions show isotopic separation. Therefore, this strategy may also be applicable to blocking the secretion of radioactive iodine in human milk. The strategy illustrates the importance of the element's isotopic composition (ratio of stable:radioactive isotopes) in the assessment of radionuclide transfer.

1.2 Fluoride (F)

Fluoride concentrations were determined in 210 samples of human milk (Ref. 54). The overall mean concentration was 7.1 ng/g (range < 2 to 97 ng/g). The fluoride concentrations correlated strongly with presence of fluoride in drinking water.

2. Alkali Metals

The alkali metals are those elements in group 1A of the periodic table, and include lithium, sodium, potassium, and cesium.

2.1 Lithium (Li)

Oral administration of lithium has been prescribed for psychiatric reasons. After ingestion, lithium is absorbed and distributed throughout the body water. In one case, daily doses of 800 mg lithium carbonate (16 mmoles) resulted in maternal serum lithium concentrations of approximately 0.8 mmoles per litre (Ref. 29). Lithium appears in breast milk at M/P concentrations of about 0.5 (Ref. 20). Breast milk concentrations have been observed to increase with dose (Ref. 29). When serum sodium levels are depleted, lithium is reabsorbed by the kidney, resulting in higher serum levels. During pregnancy, lithium is excreted more rapidly, resulting in lower serum levels (Ref. 20). In either of these circumstances, lithium intake by the breast-feeding infant may differ from that predicted by maternal dose alone.

2.2 Sodium (Na)

Sodium concentrations in human milk have been observed to vary significantly with gestational age (3, 12, and 30 days postpartum) and stage of lactation (concentrations decreased over the 30 day observation period) (Ref. 23). A diurnal variation in sodium is reported, with daytime fore milk having higher concentrations than hind milk (Ref. 21). Ingested sodium is taken up quickly into the milk (Ref. 21). However, a consistent correlation between sodium concentrations in milk and dietary intake has not been demonstrated (Ref. 23). The overall average sodium concentration in milk taken 30 days postpartum from 34 mothers was 94 mg/L (Ref. 23).

2.3 Potassium (K)

Potassium concentrations in milk have been shown to decrease as lactation becomes established, from 740 mg/L in the first five days, to 640 mg/L in the sixth to tenth days, to 550 mg/L in mature milk (Ref. 30). The overall average potassium concentration in milk taken seven days postpartum from 37 mothers was 700 mg/L (Ref. 31) and constituted approximately 20% average dietary intake. Although potassium concentrations may vary with gestational age, the effect is not consistent (Ref. 23). Like sodium, potassium concentrations are reported to show a diurnal variation (Ref. 21), and are not well correlated with dietary intake (Ref. 23).

2.4 Cesium (Cs)

Cesium is a metabolic analogue of potassium, and therefore may be expected to demonstrate similar physiological activity in passing from diet to human milk. Concentrations of Cs-137 in human milk samples taken in several U.S. cities in 1956 to 1961 were all less than 20pCi/L (Ref. 30). The overall average Cs-137 concentration in milk taken seven days postpartum from 37 mothers in two Italian hospitals was 56 pCi/L (range 5.8 to115 pCi/L), and constituted 40 to 115% the average dietary intake (Ref. 31). The quantity of Cs-137 associated with a given quantity of potassium in the milk may be six times as much as that in the diet (Ibid). Therefore the mammary gland may secrete cesium preferentially to potassium. The Cs-137 content of milk from women in Alaska ranged from 0 pCi/L (7 of 40 samples) to 220 pCi/L, with an average of 52 pCi/L for all non-zero samples (Ref. 58). Elevated levels were attributed to the consumption of native foods, such as caribou. The Cs-137 content of human milk taken from Belgian women from 1966-1968 decreased over the time period from 17 pCi/L to a steady 4 pCi/L (Ref. 59). Cs-137 concentrations in blood of breast-fed babies didn't exceed those of their mothers, whereas Cs-137 concentrations in the blood of bottle-fed babies did exceed those of their mothers (Ref. 32). The average cow's milk Cs-137 concentration at the time was 116 pCi/L; one breast milk sample's Cs-137 concentration was 36pCi/L (Ref. 32). A cesium secretion ratio of 0.3 daily intake has been assumed by one author in estimating doses from fallout for six-month old breast-fed infants (Ref. 33).

3. Alkaline Earth Metals

The alkaline earth metals are those elements in group 2A of the periodic table, and include magnesium, calcium, strontium, and radium. No information was found on radium levels in, or transfer to, human milk.

3.1 Magnesium (Mg)

Magnesium concentrations determined in milk samples taken five days postpartum from 18 Ethiopian and 23 Swedish women resulted in an overall mean of 25.5 mg/L, with no significant difference between the two nationalities (Ref. 11). Concentrations of magnesium in milk showed no correlation with the length of gestation (Ref. 23).

3.2 Calcium (Ca)

Calcium concentrations in human milk appear to vary greatly among individuals, to remain almost constant for one individual, and to be unaffected by diet (Ref. 21). Calcium concentrations determined in milk taken five days postpartum from 18 Ethiopian (9 privileged, 9 non-privileged) and 23 Swedish women were significantly different for all three groups, and ranged from 165 to 462 mg/L (Ref. 11). Calcium concentrations in milk samples taken in Denver (n=16) and Chicago (n=18) were 237 mg/L and 215 mg/L respectively (Ref. 30). The overall average calcium concentration in milk taken seven days postpartum from 46 Italian mothers was 308 mg/L, and constituted approximately 22% the average dietary intake (Ref. 31). A factor in calcium homeostasis may be exposure to sunlight, ensuring continuous synthesis of vitamin D3 (Ref. 11). Vitamin D increases the uptake of calcium from the intestine and appears to control translocation of divalent cations in a number of tissues.

3.3 Strontium (Sr)

Strontium is a metabolic analogue of calcium, and has been shown to accumulate in cow's milk. The overall average Sr-90 concentration in milk taken seven days postpartum from 46 mothers in three Italian hospitals was 0.97 pCi/L, and constituted 0.5 to 3.6% the average dietary intake (Ref. 31). The quantity of Sr-90 associated with a given quantity of calcium in the milk was always less than that in the diet (Ibid). This demonstrates apparent discrimination against Sr-90 in favour of calcium, by a factor of approximately 2.5 (Ref. 30). Other field survey data have shown similar average concentrations (geometric means) of Sr-90 in human milk samples collected from different geographical areas in North America over the same time period (1960 to 1961):0.70 pCi/L (n=10) in Toronto, 0.57 pCi/L (n=9) in Chicago, and 0.79 pCi/L (n=3) in Denver (Ref. 30). The Sr-90 content of milk from women in Alaska ranged from 0 pCi/L (17 of 40 samples) to 12 pCi/L, with an average of 3.1 pCi/L for all non-zero samples (Ref. 58). Elevated levels were attributed to the consumption of native foods, such as moose or caribou.

4. Group 3A Elements

The group 3A elements of the periodic table include gallium and indium. Radioactive isotopes of these elements are administered intravenously for the diagnosis of brain tumours or brain abscesses. This mode of exposure is not typical of environmental exposures; however, information related to element uptake by the mammary gland has been included.

4.1 Gallium (Ga)

Gallium concentrations in human milk after injection of Ga-67 citrate have been reported (Ref. 34, 35). These have shown a biological half-life of gallium in milk to be approximately nine days. The mechanism of accumulation in milk appears to be ionic replacement of calcium by competitive binding to Ca^{2+} and Mg^{2+} binding sites, such as the organic phosphate groups of casein (Ref. 19).

4.2 Indium (In)

Indium concentrations in human milk after injection of In-113 chelate complex (17.5 mCi) were 4.4 nCi/mL at 100 minutes and 2.4 nCi/mL at 21.5 hours (Ref. 36). No mechanism for uptake has been suggested.

5. Group 4A Elements

The group 4A elements of the periodic table include germanium, tin, and lead. Only information on lead was found.

5.1 Lead (Pb)

Lead concentrations in human milk have been reported to range from 2 ug/L (n=41) to 29 ug/L (n=9) (Ref. 2, 5, 7, 9). In another report, average concentrations in seven groups of samples (n=16 to 32) from different countries were 120 to 150 ug/L (Ref. 13). A recent study of lead in 210 samples of human milk found an overall mean concentration of 1.04 ng/g (range <0.05 to 15.8 ng/g), correlating most strongly with the age of house, exposure to heavy traffic, and coffee consumption (Ref. 54). The concentration of lead in milk is significantly correlated with blood concentrations , and was observed to be about 10% total blood lead or approximately equal to lead in plasma (Ref. 8). Therefore, the partitioning of lead between blood compartments appears to determine its partitioning to milk.

6. Group 5A Elements

The elements in group 5A of the periodic table include phosphorus, arsenic, antimony, and bismuth. No information was found on antimony or bismuth transfer to human milk.

6.1 Phosphorus (P)

Information on phosphorus transfer is based mostly upon the intraperitoneal administration of radioactive chromic phosphate (P-32) in the treatment of early stage ovarian cancer. It is believed that P-32 must dissociate from the chromate ion in order to migrate into general circulation, and that approximately 1% of the administered dose does so (Ref. 37). After administration of 15 mCi, P-32 activity levels in breast milk were observed to be 0.9 uCi/L after 3 days and 0.7 uCi/L after 7 days (Ref. 38). Because of dose contribution to the breast-feeding infant, recommendations have been given to suspend nursing after P-32 administration. In one diet-related study, phosphorus concentrations were observed to differ significantly between fore milk and hind milk (Ref. 23), and to decrease progressively as lactation proceeded (Ref. 53).

6.2 Arsenic (As)

Arsenic concentrations in human milk have been observed to average 0.7 ug/L (0.2 to 1.1 ug/L) in 25 samples (Ref. 39). There was no apparent decrease in arsenic concentrations with duration of lactation (Ref. 40).

7. Group 6A Elements

The elements in Group 6A of the periodic table include selenium, tellurium, and polonium. No information was found on tellurium or polonium transfer to human milk.

7.1 Selenium (Se)

Selenium is a normal constituent of human milk at concentrations of 10 to 20 ug/L. Concentrations have been shown to vary (7 to 33 ug/L in 241 subjects) with geographical distribution of selenium in forage crops (Ref. 4). Selenium concentrations in human milk were shown to decline in the first three months of lactation from 10.7 ug/L to 5.8 ug/L (n=13) when dietary selenium intake averaged 33 ug/day. A comparable study conducted when dietary selenium averaged 50 ug/day demonstrated only a slight decline from 11.8 to 10.0 ug/L (Ref. 41). Selenium concentrations are highest in colostrum and are positively correlated with the protein

content. Approximately 25% of the selenium in human milk is present as part of an enzyme (Ref. 42).

8. Transition Elements

The transition elements comprise three series of ten elements in the middle of the periodic table, including chromium, manganese, iron, nickle, copper, zinc, molybdenum, technetium, cadmium, and mercury.

8.1 Chromium

Chromium is considered an essential trace element for humans. Trivalent chromium is selectively bound to the serum protein, transferrin, which carries it throughout the body. Chromium concentrations in milk samples from a group of ten Finnish women were found to average 0.4 ug/L (range 0.19 to 0.69 ug/L in ten samples) (Ref. 43). Dietary chromium intake was analyzed to be 31 ug/day, but no correlation was found between dietary intake and chromium concentrations in milk. In a more recent study of milk from 45 American women (n=261), average chromium concentrations were 0.3 ug/L (range 0.06 to 1.56 ug/L) (Ref. 3). Although dietary chromium intake was not determined, median intake in the U.S. was reported to be 60 ug/day. These findings further supported the apparent lack of effect of dietary chromium on concentrations in human milk. Serum and urinary chromium concentrations, on the other hand, have been shown to accurately indicate daily dietary chromium intake (Ref. 12).

8.2 Manganese (Mn)

Official recommended intakes for manganese have not been given, although the World Health Organization has suggested 2 to 3 mg/day for adult males (Ref. 44). With an estimated average maternal manganese intake of 5 mg/day, the mean concentrations of manganese in human milk (n=15) were 4.5 ± 1.8 ug/L at six to eight weeks postpartum, and 4.0 ± 1.5 ug/L at 17 to 22 weeks postpartum (Ref. 24). There was a positive correlation between dietary manganese and the manganese content of milk in both weeks, but only that of the second survey week was statistically significant. It is not clear whether higher dietary intakes would result in higher manganese concentrations in milk.

In contrast to the above data, earlier work suggested manganese concentrations in human milk (n=3) to average 120 ug/L (Ref. 5). In another study, manganese concentrations in milk were observed to decrease rapidly during the first four months of lactation (Ref. 40). As the data from these studies are limited, the cause of these differences is not known.

8.3 Iron (Fe)

The mean concentrations of iron in human milk was 0.4 ± 0.1 mg/L at six to eight weeks postpartum, and significantly lower at 17 to 22 weeks postpartum at 0.29 ± 0.09 mg/L (Ref. 24). Similar results were found for milk samples taken five days postpartum from Swedish (n=23) and Ethiopian (n=18) women. The overall average iron concentration in milk was 0.48 mg/L with no significant difference between the groups (Ref. 11). There was no correlation between dietary iron and iron concentrations in the milk, even when iron supplementation was used regularly. The recommended dietary iron intake for lactating women is 16 mg/day (Ref. 45). Earlier work indicated iron concentrations in human milk (n=13) to average 0.84 mg/L (Ref. 5). However, iron in human milk is associated with the lipid fraction, and a milk sample which is not representative of the total fat in daily secretions will result in an error in iron concentration (Ref. 53).

8.4 Nickel (Ni)

Nickel is considered an essential trace element, as well as a toxic element at higher concentrations, although its effects on human metabolism are not well understood. The overall average nickel concentration observed in 179 milk samples from different countries was 0.12 mg/L (range 0.03 to 0.42 mg/L) (Ref. 13).

8.5 Copper (Cu)

Official recommended intakes for copper have not been given, although the World Health Organization has suggested 30 ug/kg/day for adult males (Ref. 44). With an estimated average maternal copper intake of 1.8 mg/day, the mean concentrations of copper in human milk (n=15) were 0.36 ± 0.07 mg/L at six to eight weeks postpartum, and significantly lower, 0.21 ± 0.017 mg/L, at 17 to 22 weeks postpartum (Ref. 24). There was no correlation between dietary copper and copper concentrations in the milk. More variable results were found for milk samples taken five days postpartum from Swedish (n=23) and Ethiopian (n=18) women. Group average copper concentrations in milk were 0.61 mg/L (Swedish), 0.37 mg/L (Ethiopian, non-privileged), and 0.17 mg/L (Ethiopian, privileged) (Ref. 11). Variations in dietary intake were not considered a likely cause, and none other was suggested; however, colostrum contains high concentrations of copper (Ref. 46). Earlier worked indicated copper concentrations in human milk (n=13) to average 0.24 mg/L (Ref. 5).

8.6 Zinc (Zn)

Recommended dietary zinc intake for lactating women is 25 mg/day (Ref. 45). With an estimated average maternal zinc intake of 13 mg/day, the mean concentrations of zinc in human milk (n=15) were 1.89 ± 0.74 mg/L at six to eight weeks postpartum, and significantly lower, 0.72 ± 0.44 mg/L, at 17 to 22 weeks postpartum (Ref. 24). There was no correlation between dietary zinc and zinc concentrations in the milk. In another study, a similar average concentration of 1.34 mg/L (n=13) was found (Ref. 5). However, much higher concentrations were found in samples (n=41) taken five days postpartum from Swedish and Ethiopian women - an overall average of 5.79 mg/L (Ref. 11). The difference may be due to high concentrations of zinc in colostrum (Ref. 46). The greatest source of variation in measurement of zinc in human milk has been attributed to individual differences among women, indicating that the number of subjects providing samples is important for representative data (Ref. 53).

8.7 Molybdenum (Mo)

Daily intakes of molybdenum by breast-feeding infants were calculated to range from 4.9 ug in the first two weeks, to 6.4 ug in the 11th to 14th weeks (Ref. 40). The concentrations of molybdenum in milk on which these calculations were based were not given. No other reference to molybdenum in human milk was found.

8.8 Technetium (Tc)

Technetium concentrations in human milk have been reported after use of a technetium radiopharmaceutical (Ref. 47, 48, 49, 50). The reports are based upon a small number of case histories, and demonstrated that injection of a technetium compound resulted in transfer to milk of approximately 0.28% the administered dose, over 90% of that in the first 18 hours. Sodium pertechnetate is distributed throughout the body like iodide (concentrated in thyroid, salivary gland, stomach, excluded from cerebrospinal fluid), but its effects are less because of a shorter half-life. Breast milk activity was attributed to free pertechnetate, although a small amount of activity became bound to breast milk protein. Inhalation of a technetium aerosol in addition to the injection resulted in very little additional breast-milk activity.

8.9 Cadmium (Cd)

Cadmium is reported to be selectively retained within mammary tissues and is therefore not secreted into milk (Ref. 51). However, a recent study of cadmium in 210 samples of human milk found an overall mean concentration of 0.08 ng/g (range <0.002 to 4.05 ng/g), correlating most strongly with exposure to cigarette smoke (Ref. 53).

8.10 Mercury (Hg)

Average mercury concentrations in human milk have been reported to range from 0.9 ± 0.2 ug/L (n=100) to 63 ug/L (n not given) (Ref. 7). Milk:plasma (M/P) ratios have also been reported to range from 0.03 to 0.9. These differences are partly due to varying proportions of organic and inorganic mercury, and are likely also due to differences in analytical techniques. It is known that organic mercury binds well (90%) to erythrocytes, and is therefore less available for transfer to milk. Inorganic mercury is distributed approximately equally between plasma and red blood cells (Ref. 7). In a methylmercury poisoning, the M/P ratio for total mercury was 0.03. Approximately 60% of the mercury in milk was organic, compared to 86% of the mercury in maternal blood (Ref. 18). Mercury concentrations in the milk of Eskimo mothers from Anchorage averaged 3.3 ug/L, and were reported to be similar to those of other women who seldom eat fish (Ref. 10). The presence of selenium may have profound protective effects on the toxicity of mercury.

9. Summary

Characteristics of element transfer to human milk which have been reported in the literature have been described. Information was available for a total of 25 elements. No reports were found for elements with atomic numbers greater than 82 (lead); therefore, there is no information on most elements of the uranium and thorium decay series. Of the 25 elements for which information was retrieved, all were reported to be secreted in human milk. The concentrations in milk were generally related to intake (except for sodium, magnesium, chromium, iron, nickel, copper, zinc) and/or body burden (lead, arsenic). However, the relationship between intake (exposure) and secretion in human milk appears to be complex, involving numerous factors which act independently on each element. Chemical similarities appear to influence the uptake of some elements (e.g. cesium and potassium, gallium and calcium, sodium and lithium), but not others (e.g. strontium and calcium). For those elements for which diet:milk concentrations have been observed, transfers range from 1% (strontium) to 20% (potassium, calcium, selenium), to as much as 600% (cesium).

There are factors which appear to influence element uptake, such as the degree of protein binding. But there are other metabolic and nutritional factors, many as yet unknown, which bring about variations in uptake associated with gestational age, duration of lactation, and time of day. Because the secretory mechanisms are not generally known, there is no simple method of predicting an element's transfer potential to human milk. Therefore, estimating transfer potential of any radionuclide will require characterization of its metabolic pathways and transfer potentials.

It is worthwhile to note that the infants' exposures to chemical substances in maternal milk are superimposed onto the neonatal body burden. For some elements to which the mother has been exposed (lead and lithium for example), the dose to the infant through breastfeeding may be substantially less than that received in utero through transplacental migration. For example, blood lead levels in one lead-exposed mother and her child during the first three weeks after birth were observed to be similar, and high compared to normal infants; whereas the mother's milk:plasma lead ratio was less than 0.1 (Ref. 7). Similar effects have been observed to occur with lithium (Ref. 20, 55) and mercury (Ref. 7).

F. SAMPLING AND ANALYTICAL METHODS

It is well recognized that the composition of human milk varies widely between women, with duration of lactation, over a twenty-four hour day,and even during a single feed. Therefore, standardized conditions of milk collection, handling, storage, and analysis are required to obtain representative and reproducible data. This is particularly important in the determination of trace elements, because the extremely low concentrations and generally limited sample sizes make it difficult to obtain reliable, quantitative data.

In planning a field survey of human milk, there are several aspects to consider:

1. Sampling For Trace Elements In Human Milk

1. What constitutes a representative milk sample?

Because of the inherent variation in human milk composition during a feed and over a twenty-four hour period, samples which are to be truly representative must be collected at every feed during the twenty-four hour period, and at several times during the feed. This sample collection protocol is particularly important for lipid-associated constituents.

2. What constitutes a suitable sample volume?

Trace elements are in low concentrations in human milk. The elements of interest in the uranium/thorium decay series can also be expected to be in extremely low concentrations in human milk. The milk sample volumes requested in a survey will be determined by the analytical method, the detection limit required, the number of duplicate analyses required for analytical quality control, and practical limitations of sampling human milk. For example, in a recent survey for several trace elements (Ref. 54), milk sample volumes required for fluoride analysis were 3 to 5 mL, for lead and cadmium analysis 10 to 15 mL. These sample volumes did not allow for replicate analyses of the same sample.

3. What constitutes a suitable number of mothers to sample?

If the objective of the study is to determine incremental element concentrations in milk from an "exposed" population, compared to that from a "non-exposed" population, then the sample population may need to be large. The number of mothers to sample for statistically significant results will be determined by the magnitude of the expected differences between concentrations observed in the study and control groups. If the objective of the study is to determine average trace element concentrations existing in a population, the sample population may be smaller. However, the size of the population will affect the statistical significance of the results.

4. How many samples should be taken from each participant?

In order to investigate effects at different stages and lactation, a longitudinal study involving samples taken periodically throughout the nursing period should be considered. However, the number of samples taken at any one stage of lactation will, practically, be limited by the good-will of the participating mothers. The number of samples required will also depend upon how many elements of interest can be determined in the same sample. In a recent survey (Ref. 54), one sample (~ 25 mL) was requested from one feed, at any time during that feed, for trace element analysis (fluoride, cadmium, and lead). The sample was then to be sub-divided into two plastic test tubes. A second sample (~ 50 mL) was also requested, to be taken at several times during the feed and the day, for halogenated hydrocarbon analysis. This survey involved 210 mothers, who were at least four weeks postpartum.

5. How should samples be collected?

Milk composition is reported to vary with sample collection methods (Ref. 56). For example, milk which is manually expressed and that which drips spontaneously during breastfeeding differ in lactose and mineral concentrations. Manual expression has sometimes been the preferred collection method (Ref. 54), because the method minimizes contamination risk by breast pump equipment. It has also been argued that the use of a breast pump empties the breast more efficiently (Ref. 56), thereby providing a larger sample. Whatever method is used must be standardized for the survey.

6. How should samples be stored and handled?

Storage and handling requirements depend upon the components to be analyzed and the analytical requirements. Effects of sample storage or handling procedures include element adherence to container wall, or migration to the lipid or aqueous phase. Several minerals (zinc, iron, copper, sodium) have been demonstrated to be unaffected by 24 hour storage in Pyrex or polypropylene containers, or 48 hour

storage at 4°C (Ref. 56). Samples collected for trace element analysis in a recent survey were collected and shipped in contamination-free polystyrene containers. Samples were frozen until 24 hours before analysis (Ref. 54). Whatever method is used must be standardized for the survey.

7. What relevant information should be gathered from the survey participants?

Data which are relevant to any survey of human milk are summarized in **Table 3**. Additional information requirements will be determined by the objective of the survey.

2. Analytical Methods for Trace Elements in Human Milk

Analytical methods for trace elements in human milk have been extremely varied. In general, whole samples (or aliquots taken from thawed, carefully mixed samples) have been prepared for analysis by ashing. Wet ashing techniques have been found more reliable than dry ashing techniques (Ref. 5). Element analysis has most commonly been done by atomic absorption spectrophotometry (AA). Flame AA has been used in the determination of copper, iron, manganese, zinc (Ref. 24), and lead (Ref. 2). In one study using flame AA, sodium chloride was added to the ash in the analysis of lead, and sodium chloride/calcium chloride were added to the ash in the analysis of manganese, to complex interferents and improve flame characteristics (Ref. 5). Flameless AA has been used in determination of total mercury (Ref. 10) and lead (Ref. 8). Flameless AA with carbon cup has been used for lead analysis (Ref. 9).

Selenium concentrations have been analyzed fluorometrically (Ref. 4) by gas chromatography with electron capture (Ref. 42), and by AA with graphite furnace and deuterium-background corrector (Ref. 41), a method which was also used for chromium analysis (Ref. 43). Chromium in human milk has also been analyzed directly without ashing by electrothermal AA (Ref. 12), as has lead (Ref. 13). Nickel in milk has been determined by inductively-coupled plasma emission spectroscopy (Ref. 13). Arsenic has been analyzed by neutron activation and radiochemical separation (Ref. 40). Sodium has been analyzed by an ion-selective procedure (Ref. 23). Radiochemical analyses have generally been done by activity counting with a liquid scintillation counter or a sodium iodide well scintillation counter. Separation of radioisotopes, Sr-90 and Cs-137 for example, was done in one study by a standard ion exchange technique prior to activity counting (Ref. 31).

As can be seen from the above, a variety of methods have been used for elemental and radiochemical analyses of human milk samples. None of these has been standardized. Therefore, in planning any survey, analytical method development is first recommended. Its purpose would be to establish analytical methods with adequate detection limits, which are suitable for biological samples such as human milk. The accuracy and precision of the methods are to be characterized at the

Table 3. Relevant sampling information

1. Number of subjects, samples.
2. Mother's age, race, occupation, geographic location (length of residence).
3. Primapara or other.
4. Full term or pre-term (gestational age), normal delivery or other.
5. Duration of lactation.
6. Stage of feeding(- foremilk - midmilk - hindmilk - left - right breast).
7. Time of year.
8. Smoking habits in home (all family members).
9. State of nutritional health (estimated consumption rates of particular foods may be desirable).
10. Mother's use of drugs or medication, during pregnancy and since birth.
11. Method for determining mother's exposure to chemical(s) of interest.
12. Method for determining infant's milk intake.

concentrations of analyte expected in the samples. These characteristics must be established in advance, to ensure that the analytical methods of choice meet the investigatory requirements.

When the analytical methods are characterized, detailed standardized sampling and analytical protocols can be developed. A quality control programme (and procedures) is a necessary and integral part of the protocols. It should include routine procedures for determining:

(1) Accuracy
- by analysis of a standard biological reference material, such as cow's milk;

(2) Recovery
- by method of standard addition to standard reference material; cross-check with replicate analyses by other laboratories on a regular basis;

(3) Reproducibility
- by preparing standard curves daily in the concentration range of the analyte expected;
- by replicate analysis of pooled sample;

(4) Field, Lab or Procedural Contamination
- by use of field and reagent blanks;
- by repeating (simulating) collection method using pooled samples, and processing as standard sample;
- reference standards and blanks interspersed with samples

3. Food Sampling and Analysis

The discussion thus far has focussed upon the sampling and analysis of human milk. In assessing element transfer from the environment to human milk, some consideration should be given to the evaluation of maternal exposures. In the studies reviewed for this report, most did not estimate or determine maternal exposures. The few which did (summarized in Appendix 1) used various methods of estimating element intake by food. The most specific of these was the use of food diaries combined with sampling and analysis of representative meals. Food samples were homogenized, ashed, and analyzed by methods similar to those used for human milk samples. Contamination of the food sample by processing methods (e.g. steel blades of the homogenizer) was checked. If food diaries and food samples are used, it is advisable to correlate analytical results from food samples with results calculated from food diaries, so that the accuracy of calculated estimates can be validated.

G. SUMMARY AND CONCLUSIONS

In order to evaluate the significance of human milk to the total dose commitment of the breast-feeding infant, a literature review was conducted to assess elemental transfer from the environment to human milk. Of the 25 elements for which relevant information was found, Sr-90, Cs-137 and radiopharmaceuticals were the only radioisotopes discussed. The only element in the uranium and thorium decay series for which information was available was lead (Pb). From the transfer characteristics of the 25 elements, it appears that there is no simple method for predicting an element's transfer potential to human milk.

Therefore, to evaluate the significance of this pathway in a risk assessment of the nuclear fuel cycle, more data such as that which can be collected in a field survey are necessary. However, before a field survey can be initiated, program planning must allow for:

(i) selection of the elements (radioisotopes) of interest;

(ii) development of appropriate analytical methods for the concentrations of radioisotopes of interest expected in human milk;

(iii) development of standardized sampling and analytical protocols, including quality control requirements; and

(iv) identification of statistical treatment for the survey data.

In the absence of survey data, the dose to the breast-feeding infant can only be estimated, based upon assumptions of transfer characteristics of similar elements.

H. REFERENCES

1. BRUHN, J.C. and A.A. FRANKE (1983). Iodine in human milk. J. Dairy Sc. 66 : 1396-1398.

2. DILLON, H.K., D.J. WILSON, W. SCHAFFNER (1974). Lead concentrations in human milk. Am J. Dis. Child 128 : 491-492.

3. CASEY, C.E., K.M. HAMBIDGE (1984). Chromium in human milk from American mothers. Br. J. of Nutr. 52 : 73-77.

4. SHEARER T.R., D.M. HADJIMARKOS (1975). Geographic distribution of selenium in human milk. Arch. Env. Health 30 : 230-233.

5. MURTHY, G.K., U.S. RHEA (1971). Cadmium, copper, iron, lead, manganese, and zinc in evaporated milk, infant products, and human milk. J. Dairy Science 54 (7) : 1001-1005.

6. LONNERDAL, B., M. CLEGG, L.S. HURLEY (1981). Changes in concentration and distribution of trace elements in human milk during lactation. Am. J. Clin. Nutr. 34 (4) :641.

7. WOLFF, M.S. (1983). Occupationally derived chemicals in breast milk. Am. J. Ind. Med. 4 : 259-281.

8. MOORE, M.R., A. GOLDBERG, S.J. POCOCK, A. MEREDITH, I.M. STEWART, H. MACANESPIE, R. LEES, A. LOW (1982). Some studies of maternal and infant lead exposure in Glascow. Scot. Med. J. 27 : 113-122.

9. HUAT, L.H., D. ZAKARIYA, K. HOON (1983). Lead concentrations in breast milk of Malaysian urban and rural mothers. Arch. Env. Health 38 (4) :205-209.

10. GALSTER, W.A. (1976). Mercury in Alaskan Eskimo mothers and infants. Env. Health Perspectives 15 : 135-140.

11. FRANSSON, G.B., M. GEBRE-MEDHIN, L. HAMBRAEUS (1984). The human milk contents of iron, copper, zinc, calcium, and magnesium in a population with a habitually high intake of iron. Acta Paediatr. Scand. 73 : 471-476.

12. KUMPULAINEN, J., J. LEHTO, P. KOIVISTOINEN, M. UUSITUPA, E. VUORI (1983). Determination of chromium in human milk, serum, and urine by electrothermal atomic absorption spectrometry without preliminary ashing. The Science of the Total Environment 31:71-80.

13. CAMARA, RICA C., G.F. KIRKBRIGHT (1982). Determination of trace concentrations of lead and nickel in human milk by electrothermal atomization, atomic absorption, spectrophotometry and inductively-coupled plasma emission spectroscopy. The Science of the Total Environment 22 : 193-201.

14. IMPERATO, C. and E. FERRANTE (1981). Drugs and environmental pollutants in maternal milk. Minerva Pediatrica 33 (9) : 377-384.

15. OVCHARENKO, E.P. (1982). Radionuclide uptake in progeny. Medical Radiology (Moscow), 27 (1) : 71-78 January.

16. BERLIN, C.M. (1981). Pharmacologic considerations of drug use in the lactating mother. Obstetrics and Gynecology 58 (5) Supplement : 175-235.

17. SANDSTROM, B., A. CEDERBLAD, B. LONNERDAL (1983). Zinc absorption from human milk, cow's milk and infant formulas. Am. J. Dis. Child 137 : 726-729.

18. AMIN-ZAKI, L., S.B. ECHASSANI, M.A. MAJEED, T.W. CLARKSON, R.A. DOHERTY, M.R. GREENWOOD (1980). Methylmercury poisoning in mothers and their suckling infants. Dev. Toxicol Env. Sci. 8 : 75-78.

19. ANGHILERI, L.J., M. HEIDBREDER (1976). On the accumulation of Ga-67 in human breast milk: probable mechanism. The Journal of Nuclear Biology and Medicine 20 (4) :179.

20. LINDEN, S., C. L. RICH (1983). The use of lithium during pregnancy and lactation. J. of Clinical Psychiatry 44 (10) :358-361.

21. GUNTHER, M. (1968) Diet and milk secretion in women. Proc. Nutr. Soc. (Eng.). 27 (1) :77-82 March.

22. POSTELLON, D.C., R. ARONOW (1982). Iodine in mother's milk. JAMA 247 (4) : 463.

23. BOOK, L.S., G.M. CHAN, M.R. THOMAS (1984). Effect of gestational age maternal diet and sampling time on human milk mineral content. Pediatric Research18
(4 PART 2) : 190A.

24. VUORI, E., S.M. MAKINEM, R. KARA, P. KUITUNEN (1980). The effects of the dietary intakes of copper, iron, manganese, and zinc on the trace element content of human milk. Am. J. Clin. Nutr. 33 : 227-231.

25. GUSHURST, C.A., J.A. MUELLER, J.A. GREEN, F. SEDOR (1984). Breast milk iodide: reassessment in the 1980's. Pediatrics 73 (3) :354-357.

26. MURAMATSU, Y., M. SUMIYA, Y. OHMOMO (1982). Iodine contents in human milk in relation to algae consumption by mother. J. Radiat. Res. 23 (1) : 81.

27. WYBURN, J.R. (1973). Human breast milk excretion of radionuclides following administration of radiopharmaceuticals. J. Nucl. Med. 14 (2) :115-117.

28. VEALL, N., T. SMITH (1980). Excretion of I-125 in breast milk following administration of labelled fibrinogen. Br. J. Radiology 53 : 512-513.

29. SYKES, P.A., J. QUARRIE, F.W. ALEXANDER (1976). Lithium carbonate and breast-feeding. British Medical Journal 27 November : 1299.

30. STRAUB, C.P., G.K. MURTHY (1965). A comparison of Sr-90 component of human and cow's milk. Pediatrics 36 (5) :732-735.

31. CALAPAJ, G.G., D. ONGARO (1970). Observed ratios of Sr-90/Ca and Cs-137/K in the food of nursing mothers and in their milk. J. Dairy Res. 37 :1-7.

32. RUNDO, J. (1970). Fall-out cesium-137 in breast - and bottle-fed infants. Health Physics 18 (4) : 437-438.

33. UCHIYAMA, M. (1982). Collective doses to infants in Chiba-city internally exposed to fallout Cs-137 for the first 6 months after birth. J. Radiation Res. 23 (1) : 54-5.

34. LARSON, S.M., G.L. SCHALL (1971). Gallium 67 concentration in human breast milk. JAMA 218 (2) : 257.

35. TOBIN, R.E., P.B. SCHNEIDER (1976). Uptake of Ga-67 in the lactating breast and its persistence in milk: case report. J. Nucl. Med. 17 : 1055-1056.

36. PULLAR, M., A. HARTKAMP (1977). Excretion of radioactivity in breast milk following administration of an indium -113m labelled chelate complex. Br. J. of Radiology 50 (599) : 846.

37. CARLSON, J.A., B. JOSE, S.C. SHARMA, R.P. OSBORN (1983). Radioactivity in breast milk after intraperitoneal chromic phosphate for the treatment of early ovarian cancer. Am. J. Obstet. Gynecol. 147 (7) : 840-841.

38. SHARMA, S.C., R.P. OSBORNE, B. JOSE, J.A. CARLSON (1984). Dose estimation to the infant from breast milk following intraperitoneal administration of chromic phosphate P-32 for the treatment of early ovarian cancer. Health Physics 47 (3) : 452-454.

39. DANG, H.S., D.D. JAISWAL, S. SOMASUNDARAM (1983). Distribution of arsenic in human tissues and milk. The Science of the Total Environment 29 : 171-175.

40. DANG, H.S., D.S. JAISWAL, C.N. WADHWANI, H. DACOSTA, S. SOMASUNDARAM (1983). Intake of trace elements by Indian infants through breast milk and commercial milk formula. In Trace Element - Analytical Chemistry in Medicine and Biology. Vol. 2, Walter de Gruyter and Co., N.Y.

41. KUMPULAINEN, J., E. VUORI, M.A. SIIMES (1984). Effect of maternal dietary selenium intake on selenium levels in breast milk. Internat. J. Vit. Nutr. Res. 54 : 251-255.

42. SMITH, A.M., M.F. PICCIANO, J.A. MILNER (1982). Selenium intakes and status of human milk and formula fed infants. Am. J. Clin. Nutr. 35 : 521-526.

43. KUMPULAINEN, J., E. VUORI, S. MAKINEN, R. KARA (1980). Dietary chromium intake of lactating Finnish mothers: effect on the Cr content of their breast milk. Br. J. Nutr. 44 : 257-263.

44. WHO 1973. World Health Organization Expert Committee In: Trace Elements in Human Nutrition. WHO Tech. Report Series 532 : 17-18, 34-35, Geneva.

45. NAS 1973. National Academy of Science, Recommended Daily Dietary Allowances. Food and Nutrition Board, NAS, NRC, Nutr. Rev. 31 : 395 (1973).

46. PREMA, K. (1978). Pregnancy and lactation: some nutritional aspects. Indian J. Med. Res. 68 (Suppl.) : 70-79.

47. MOUNTFORD, P.J., F.M. HALL, C.P. WELLS, A.J. COAKLEY (1984). Breast milk radioactivity after a Tc-99m DTPA aerosal/Tc-99m MAA lung study. J. Nuclear Medicine 25 : 1108-1110.

48. OGUNLEYE, O.T. (1983). Assessment of radiation dose to infants from breast milk following the administration of Tc-99 pertechnetate to nursing mothers. Health Physics 45 (1) : 149-151.

49. PITTARD, W.B., K. BILL, B.D. FLETCHER (1979). Excretion of technetium in human milk. J. of Pediatrics 94 (4) :605-607.

50. HEATON, B. (1979). The build up of technetium in breast milk following the administration of Tc-99 O4 labelled macroaggregated albumin. British J. of Radiology 52 : 149-50.

51. SCANLON, J. (1972). Human fetal hazards from environmental pollution with certain non-essential trace elements. Clinical Pediatrics 11(3) : 135-141.

52. ADAMOVIC, V.M., B. SOKIC, M.J. SMILJANSKI (1978). Some observations concerning the ratio of the intake of organochlorine insecticides through food and amounts excreted in the milk of breast-feeding mothers. Bull. Env. Contam. Toxicol. 20 : 280-285.

53. PICCIANO, M.F. (1984). What constitutes a representative milk sample? J. Pediatric Gastroenterology and Nutrition 3 : 280-283.

54. DABEKA R.W., K.F. KARPINSKI, A.D. MCKENZIE, C.C. BAJDIK (1985). Survey of lead, cadmium and fluoride in human milk and correlation of levels with environmental and food factors. Internal report of Food Directorate, Health Protection Branch, Health and Welfare Canada.

55. SYKES P.A., J. QUARRIE, F.W. ALEXANDER (1976). Lithium carbonate and breast-feeding. British Medical Journal : 1299, 27 Nov. 1976.

56. HAMOSH M., S. BERKOW, J. BITMAN, L. FREED, B. HAPP, J.B. JONES, N.R. MEHTA, D.L. WOOD, P. HAMOSH (1983). Handling and storage of human milk specimens for research. J. Pediatric Gastroenterology and Nutrition 3 : 284-289.

57. MES, J. and R.W. DABEKA (1981). Protocol for a study of chemical residues in human milk. Internal publication, Bureau of Chemical Safety, Health Protection Branch, Health and Welfare Canada.

58. BAKER, B.F., C.H. NEILSON, E.R. SAMUELS. Strontium -90 and cesium -137 in human and other milks collected in Alaska. J. Dairy Science 53(2):241

59. VERSELE-DE CLERCQ, H., J. GILLARD-BARUH (1974). Contamination du lait humain en cesium -137 et strontium -90 en belgique, de 1966 à 1968. J. Belge de Radiologie 57(2):129-135.

APPENDIX 1

Ref. 10:

1. Element Studied: Mercury

2. Population sampled: Thirty-eight (38) Eskimo women in hospital in Anchorage and Bethel for delivery.

   # samples: n=38

3. Quantitation of intake: Consumption determined by standard questionnaire. Participants subsequently grouped by intake quantities of seed oil, seal meat, fish and birds.

4. Sampling method: None given. Milk taken a few days after delivery.

5. Analytical methods: Digestion in nitric/sulphuric acids. Flameless AA.

6. Quality control: Duplicate analyses. Standard addition analyses. Paired analyses with outside laboratory.

7. Treatment of results: Student t-test for significant difference between groups. One-way analysis of covariance for relationships between parameter. Data grouping for relationship between diet and Hg levels.

8. Conclusions of authors: No consistent pattern in Hg accumulation in milk. Average levels in milk urban mothers similar to those of women who seldom eat fish.

Ref. 23:

1. Element studied: Calcium, phosphorus, potassium, sodium

2. Population sampled: 19 mothers of term infants and 15 mothers of preterm infants.

   # samples: n = 204 (estimated from description given by authors)

3. Quantitation of intake: Calculated from diet records.

4. Sampling methods: Fore and hind milk was collected three times a day at 3, 12, and 30 days postpartum. No other information given.

5. Analytical methods: Not given

6. Quality control: Not given

7. Treatment of results: Group results averaged for fore and hind milk.

8. Conclusions of authors: Sodium concentrations were higher in preterm than term group. Calcium and phosphorus concentrations reported to be significantly higher in fore and hind milk (although data given doesn't appear to support this conclusion). Calcium, potassium, and phosphorus concentrations were higher in preterm than term in only one of three sampling days.

Ref. 24:

1. Element studied: Copper, iron, manganese, zinc

2. Population sampled: Fifteen lactating women during 6th to 8th week and 17th to 22nd week postpartum.

   # samples: n= 30

3. Quantitation of intake: Two 7-day food records were kept, to calculate average daily nutrient intake. Also, food mixtures representing each survey week were analyzed.

4. Sampling method: Milk aliquots (8 mL) collected at beginning and end of each feed, and person's samples in one 24 hour period pooled.

5. Analytical methods: Samples dry-ashed, analyzed by flame AA.

6. Quality control: Accuracy tested using standard reference material (bovine liver). Precision tested by repeated analysis of pooled samples.

7. Treatment of results: Linear correlation determined between diet and levels in milk

8. Conclusions of authors: Correlation between analyzed and calculated nutrient intakes significant. Intakes of Cu, Fe, Zn have no effect on milk concentrations (at levels observed). Mn intake did affect milk concentrations, although why (statistical effect or concentration effect) not known.

Ref. 31:

1. Element studied: Strontium-90, calcium, cesuim-137, potassium

2. Population sampled: 46 women (9, 16, 14, and 7 in 4 experiments)

samples: n = 4

3. Quantitation of intake: Diet was controlled for 4 days prior to sampling. Individual food types consumed during the period were analyzed.

4. Sampling methods: Equal volumes of milk from each mother were taken the night of the 7th and 8th day postpartum, and pooled to form a single 1000 mL group sample.

5. Analytical methods: Sr-90 and Cs-137 were separated chemically by ion exchange techniques, and complexes of the individual isotopes or daughter products determined by activity counting in a G.M. flow (Sr-90) or sodium iodide well scintillation counter (Cs-137). Ca and K were determined by wet chemical methods.

6. Quality control: None given

7. Treatment of results: Calculated average daily intake of individual elements, and determined Sr-90/Ca and Cs-137/K ratios in food and human milk. Then calculated "observed ratio" (OR) i.e. ration in milk: ratio in food.

8. Conclusions of authors: Sr-90/Ca OR always less than unity and less than 4% dietary Sr excreted in milk. Therefore, some protective mechanism limits the uptake of Sr into milk. Cs-137/K OR always greater than unity, varying widely, and 40%-115% dietary Cs excreted in milk. Therefore, no discrimination between Cs and K.

Ref. 41:

1. Element studied: Selenium

2. Population sampled: Thirty-one lactating women, after 1, 2 and 3 month's lactation.

samples n=46

3. Quantitation of intake: Method not stated although average daily intake during lactation is given. Determination appears to have been reported in a reference.

4. Sampling methods: Several feedings pooled for individual samples of several hundred grams. Sub-samples (10 mL) transferred to acid-washed polyethylene tubes and frozen.

5. Analytical methods: Milk samples heated to 40 C, mixed, sub-sampled (2 mL) for wet digestion, chelated, extracted, and analyzed by AA (graphite furnaces).

6. Quality control: Method validity and standard reference material tested.

7. Treatment of results: Significant differences between milk concentrations tested at different periods of lactation in this and a previous survey.

8. Conclusions of authors: With dietary intakes of 50 ug Se/day, breast milk selenium does not decline strongly during three months postpartum, as occurs with dietary intakes 30 ug Se/day. Therefore, adequate daily Se intake of 50 ug/day appears to be sufficient for lactating women.

Ref. 5:

1. Element studied: Chromium

2. Population sampled: 45 lactating women at varying stages up to 48 weeks postpartum.

   # samples: n=261

3. Quantitation of intake: Median national dietary intake.

4. Sampling methods: Milk was collected at a variety of times, from both breasts at mid-feed. Also, 20 women collected fore-, mid-, and hind-milk samples from a mid-morning feed. After thorough shaking, 0.5 ml milk taken, stored at -70 C in microcentrifuge tube.

5. Analytical methods: Atomic absorption spectrophotometer with graphite furnace, after wet ashing.

6. Quality control: Accuracy by method of standard additions. Precision by replicate analysis. Day-to-day coefficient of variation by analyzing pooled sample daily. Check for contamination. Analysis of two reference materials from IAEA (powdered milks - bovine and human).

7. Treatment of results: Effects of duration of lactation examined by grouping values for samples collected mid-feed, mid-morning from the right breast.

8. Conclusions of authors: Mean Cr content 0.3 ug/L did not change with duration of lactation. Results similar to concentrations reported in another study, although dietary intake (national average) is twice as high. Estimated daily Cr loss in milk at one month was 0.2 ug/day. Analytical method was rapid and convenient.

Ref. 43:

1. Element studied: Chromium

2. Population sampled: Ten lactating women in Finland, during 6th to 8th week and 17th and 22nd week postpartum.

   # samples: n = 10

3. Quantitation of intake: Two 7-day food records were kept to calculate average daily intake. Thirty (30) diet samples analyzed chemically.

4. Sampling method: Milk collected at beginning and end of each feed over 24 hour period and pooled by individual. Samples frozen.

5. Analytical methods: Food: Homogenized, dried, dry-ashed, analysis by atomic absorption (AA) - graphite furnace. Milk: Samples heated to 40 C, mixed, sub-samples taken and air-dried, dry-ashed, dissolved in H202, dissolved in HCL, analyzed by AA-graphite furnace.

6. Quality control: Recovery by method of standard addition. Precision by repeated analysis of pooled samples. Accuracy using standard reference material (bovine liver). Diet samples analyzed in triplicate. Graphite furnace checked for volatile chromium. Food samples contamination by homogenize blades checked.

7. Treatment of results: Linear correlation between diet and milk concentration.

8. Conclusions of authors: Important to use low Cr blades in homogenizer. Chromium intake does not have an effect on human milk concentration.

Ref. 52:

1. Element studied: DDT and derivatives

2. Population sampled: Two groups of five lactating mothers - one group feeding twins, second group feeding.

samples: n=70

3. Quantitation of intake: Chemical analysis of seven daily meals.

4. Sampling methods: Five (5) samples taken by each mother over 24 hours pooled. Samples taken over 7 days. No other details given.

5. Analytical methods: Food: Homogenized, dried, extracted, extract cleaned, and eluants concentrated, analyzed by gas-liquid chromatography (GLC). Milk: Deproteinized by ethanol, centrifuged, extracted, extracts combined and evaporated to dryness, redissolved, cleanup, eluant concentrated, analyzed by GLC.

6. Quality control: None given

7. Treatment of results: Results given in daily group averages.

8. Conclusions of authors: Newborn's intake of DDT through mother's milk is significant. Mothers of twins excrete similar concentrations of DDT as mothers of one.